

Amendments to the Claims

This listing of claims is marked to show changes to the immediate prior version of claims pending in this application, and will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-36. (Canceled)

Claim 37. (Currently Amended) A transdermal antigenic composition, comprising at least 4 components, which are:

- (a) a transdermal carrier comprising a penetrant suspended or dispersed in an aqueous solvent,

the penetrant being in the form of a minute fluid droplet surrounded by a coating of one or more layers of at least 2 substances that differ by at least a factor of 10 in solubility,

the substances forming homoaggregates of one substance and/or heteroaggregates of the at least 2 substances, the average diameter of homoaggregates of the more soluble substance, or the average diameter of the heteroaggregates of the at least 2 substances, being smaller than the average diameter of homoaggregates of the less soluble substance, and/or

the more soluble substance solubilizing the droplet and the content of the more soluble substance being up to 99 mol-% of the concentration required to solubilize the droplet or corresponding to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or

wherein the elastic deformation energy of the droplet surrounded by the coating is at least 5 times lower than the elastic deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains;

- (b) a compound which specifically has or induces cytokine or anti-cytokine activity;
- (c) an antigen or mixture of different antigens and/or an allergen or mixture of different allergens; and
- (d) a chemical irritant, ~~an extract or a compound from a pathogen, a fragment or a derivative of the chemical irritant, or compound isolated from a pathogen.~~

Claim 38. (Previously presented) The antigenic composition of claim 37, wherein the at least two substances are two ionization states or salt forms of the same substance.

Claim 39. (Canceled).

Claim 40. (Previously presented) The antigenic composition according to claim 37, wherein the less soluble substance with the tendency to aggregate is a polar lipid, and the more soluble substance is a surfactant.

Claim 41. (Previously presented) The antigenic composition according to claim 37, wherein the average diameter of the penetrant is between 30 nm and 500 nm.

Claim 42. (Previously presented) The antigenic composition according to claim 37, wherein the total weight of droplets in the antigenic composition for use on human or animal skin is 0.01 weight-% (w-%) to 40 w-% of total mass of the antigenic composition.

Claim 43. (Previously presented) The antigenic composition according to claim 37, wherein the total antigen concentration is between 0.001 and 40 w-% of the total penetrant mass.

Claim 44. (Canceled)

Claim 45. (Previously presented) The antigenic composition according to claim 37, wherein the compound is IL-4, IL-3, IL-2, TGF, IL-6, IL-7, TNF, IL-1a and/or IL-1b, IL-12, IFN-g, TNF-b, IL-5, IL-10, a type I interferon, IFN-alpha, or IFN-b.

Claim 46. (Withdrawn – Currently Amended) The antigenic composition according to claim 37, wherein the compound is an anti-cytokine antibody or an active fragment, ~~a derivative, or an analog~~ thereof.

Claim 47. (Currently Amended) The antigenic composition according to claim 37, wherein the antigen is ~~derived~~ from a pathogen.

Claim 48. (Previously presented) The antigenic composition according to claim 47 wherein said pathogen is selected from the group consisting of extracellular bacteria, gram-negative bacteria, gram-positive bacteria, bacteria and viruses, which survive and replicate within host cells, fungi prospering inside host cells, parasites, the causative agent for cholera, *Haemophilus* species, pathogens triggering paratyphoid, pathogens triggering plague, pathogens triggering rabies, *Clostridium tetani*, pathogens triggering rubella, and pathogens that cause various neoplasiae, auto-immune diseases or are related to other pathological states of the animal or human body which do not necessarily result from pathogen infections.

Claim 49. (Withdrawn – Currently Amended) The antigenic composition according to claim 37, wherein the allergen is of xenogenic or endogenic origin; ~~derived~~ from a microorganism, an animal or a plant; a man made and/or irritating inorganic substance; or a part or component of the human body which was incorrectly processed by or exposed to the body immune system.

Claim 50. (Previously presented) The antigenic composition according to claim 37, wherein the concentration of the compound used is up to 1000 times higher than a concentration optimum established in corresponding tests performed by injecting the antigenic compositions or performing the tests in vitro.

Claim 51. (Canceled)

Claim 52. (Canceled)

Claim 53. (Canceled)

Claim 54. (Canceled)

Claim 55. (Canceled)

Claim 56. (Withdrawn – Currently Amended) The antigenic composition according to claim 37, ~~further comprising an wherein the~~ irritant is selected from the classes of allergenic metal ions, acids, bases, irritating fluids, (fatty-) alcohols, (fatty-) amines, (fatty-) ethers, (fatty-) sulphonates, or –phosphates or ~~derivatives~~ or combinations thereof.

Claim 57. (Withdrawn – Currently Amended) The antigenic composition according to claim 37, ~~further comprising an wherein the~~ irritant that is a solvent or amphiphile ~~or a derivative~~ or combination thereof.

Claim 58. (Currently Amended) The antigenic composition according to claim 37, ~~further comprising an~~ wherein the irritant is selected from the group consisting of surfactants ~~and derivatives~~ and combinations thereof.

Claim 59. (Previously presented) The antigenic composition according to claim 58 wherein the surfactant enhances skin permeation.

Claim 60. (Previously presented) The antigenic composition according to claim 37, wherein the concentration of the irritant is below by at least a factor of 2 to a factor of 10 or more a concentration which is unacceptable owing to local irritation in tests on the same or a comparable subject.

Claim 61. (Withdrawn – Previously presented) The antigenic composition according to claim 37, wherein the allergen is an inhalation allergen, food allergen, drug allergen, contact allergen, injection allergen, invasion allergen, or depot allergen.

Claim 62. (Previously presented) The antigenic composition according to claim 37, wherein the applied dose of the antigen differs by the factor of 0.1 to 100 from the dose which would have to be used with an injection.

Claim 63. (Previously presented) The antigenic composition according to claim 37, wherein the applied dose of an antigen is less than 10 times higher than the dose which would have to be used with an injection.

Claim 64. (Previously presented) The antigenic composition according to claim 37, wherein the applied penetrant dose is between 0.1 mg/cm^2 and 15 mg/cm^2 .

Claim 65. (Previously presented) The antigenic composition according to claim 37, wherein the antigen is a pure or purified antigen.

Claim 66. (Previously presented) A kit, comprising at least one dose of the antigenic composition according to claim 37 in packaged form.

Claim 67. (Canceled)

Claim 68. (Withdrawn – Currently Amended) A method for generating a protective immune response in a mammal by comprising the step of administering to the mammal an antigenic composition according to claim 37.

Claim 69. (Withdrawn – Previously presented) The method according to claim 68, wherein a suspension of antigen-free penetrants is loaded with the antigen to be associated therewith about 30 minutes before administration of the antigenic composition.

Claim 70. (Withdrawn – Previously presented) The method according to claim 68, wherein the antigenic composition is applied on skin after pre-treating the skin by an immunoadjuvant manipulation, the manipulation comprising rubbing, pressing, heating, exposing to an electrical or mechanical field, or injecting a non-immunogenic formulation in the skin, wherein such treatment releases immunoadjuvant compounds from the skin or other peripheral immunoactive tissues or reduces the concentration of antagonists to the desired vaccination and/or the duration of action of said antagonists.

Claim 71. (Withdrawn) The method according to claim 68 wherein immunogen is applied in a non-occlusive patch.

Claim 72. (Withdrawn – Previously presented) The method of claim 68 wherein at least one dose of antigenic composition is administered.

Claim 73. (Withdrawn – Previously presented) The method according to claim 72, wherein the antigenic composition is administered as a booster vaccination.

Claim 74. (Withdrawn) The method according to claim 73, wherein a primary immunization is done invasively and wherein the booster immunization is done non-invasively.

Claim 75. (Withdrawn – Previously presented) The method according to claim 68, wherein the antigenic composition is applied between 2 and 10 times when a non-allergenic antigen is used.

Claim 76. (Withdrawn – Previously presented) The method according to claim 75, wherein the time interval between subsequent administrations is between 2 weeks and 5 years.

Claim 77. (Withdrawn – Currently Amended) A method for inducing a protective or tolerogenic immune response comprising administering an antigenic composition, the antigenic composition comprising at least 4 components, which are:

- (a) a transdermal carrier comprising a penetrant suspended or dispersed in an aqueous solvent, the penetrant being in the form of a minute fluid droplet surrounded by a coating of one or more layers of at least 2 substances that differ by at least a factor of 10 in solubility,

the substances forming homoaggregates of one substance and/or heteroaggregates of the at least 2 substances, the average diameter of homoaggregates of the more soluble substance, or the average diameter of the heteroaggregates of the at least 2 substances, being smaller than the average diameter of homoaggregates of the less soluble substance, and/or

the more soluble substance solubilizing the droplet and the content of the more soluble substance being up to 99 mol-% of the concentration required to solubilize the droplet or corresponding to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or

wherein the elastic deformation energy of the droplet surrounded by the coating is at least 5 times lower than the elastic deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains;

- (b) a compound which specifically has or induces cytokine or anti-cytokine activity;
- (c) an antigen or mixture of different antigens and/or an allergen or mixture of different allergens; and
- (d) a chemical irritant, ~~an extract or a compound from a pathogen, a fragment or a derivative of the chemical irritant, or compound isolated from a pathogen.~~

Claim 78. (Canceled)

Claim 79. (Canceled)

Claim 80. (Currently Amended) A transdermal antigenic composition, comprising at least 4 components, which are:

- (a) a transdermal carrier comprising a penetrant suspended or dispersed in an aqueous solvent,

the penetrant being in the form of a minute fluid droplet surrounded by a coating of one or more layers of at least 2 substances that differ by at least a factor of 10 in solubility,

the substances forming homoaggregates of one substance and/or heteroaggregates of the at least 2 substances, the average diameter of homoaggregates of the more soluble substance, or the average diameter of the heteroaggregates of the at least 2 substances, being smaller than the average diameter of homoaggregates of the less soluble substance,

and/or

the more soluble substance solubilizing the droplet and the content of the more soluble substance being up to 99 mol-% of the concentration required to solubilize the droplet or corresponding to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or

wherein the elastic deformation energy of the droplet surrounded by the coating is at least 5 times lower than the elastic deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains;

- (b) a compound which specifically has or induces cytokine or anti-cytokine activity; ~~and~~
- (c) an antigen or mixture of different antigens and/or an allergen or mixture of different allergens; and
- (d) a chemical irritant;

wherein said (b) and (c) are associated with the penetrant, and wherein said composition is to provide a protective or tolerogenic immune response.

Claim 81. (Currently Amended) The composition of claim 80, wherein (c) comprises a part of a pathogen or an allergen in its natural form or after fragmentation ~~or derivatisation~~.

Claim 82. (Canceled)

Claim 83. (Previously presented) The composition of claim 80, wherein to provide said protective immune response is to provide complete protection against a normally lethal challenge.

Claim 84. (Previously presented) The composition of claim 37, wherein said composition is to provide a protective or tolerogenic immune response.

Claim 85. (Previously presented) The composition of claim 37, wherein said composition is to provide a protective immune response.

Claim 86. (Previously presented) The composition of claim 80, wherein said composition is to provide a protective immune response.

Claim 87. (Canceled)

Claim 88. (Canceled)